10

CLAIMS

What I claim is:

1. A method of neoadjuvant chemotherapy in patients with inflammatory breast cancer or T3 or T4 breast cancer which comprises administering to said patient a plurality of cycles of chemotherapy at predetermined intervals until cancerous tissue is reduced to an operable size or is in remission, wherein each said cycle comprises:

(a) first administering to said patients at least one diphenyl compound of the formula:

$$\begin{array}{c|c} & & & \\ & & & \\ X_p & & & \\ & & & \\ X_p & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$$

wherein X and Y are each fluorine, chlorine or bromine, Z is an alkylene group of 1 to 3 carbon atoms or =C=O, or the phenyl groups are joined to form a tricyclic ring, o and p are 0 or 1, R_1 and R_2 are each an alkyl group containing 1 to 3 carbon atoms or are joined together to form a heterocyclic ring with the nitrogen atom and n is 1, 2 or 3, or pharmaceutically-acceptable salts thereof, and

- (b) following sufficient time to permit inhibition of binding of intracellular histamine, subsequently administering to the patient an anthracycline chemotherapeutic agent and a taxane chemotherapeutic agent.
- 2. The method of claim 1 wherein the group

$$-N$$
 R_1
 R_2

is a diethylamino group, a dimethylamino group, a morpholino group or a piperazino group.

3. The method of claim 1 wherein the group

$$-N$$
 R_1

is a diethylamino group, Z is -CH₂, n is 2 and o and p are each 0.

WO 2004/022163

- 4. The method of claim 3 wherein diphenyl compound is in the form of a hydrochloride salt.
- 5. The method of claim 1 wherein said anthracycline chemotherapeutic agent is doxorubicin or epirubicin.
- 6. The method of claim 4 wherein said anthracycline chemotherapeutic agent is doxorubicin or epirubicin.
- 7. The method of any one of claim 1, 4, 5 and 6 wherein said taxane chemotherapeutic agent is Taxol or Taxotere.
- 8. The method of claim 1 wherein said diphenyl compound is administered to the patient about 30 to about 90 minutes prior to said administration of said chemotherapeutic agents.
- 9. The method of claim 8 wherein said time is about 60 minutes.
- 10. The method of claim 7 wherein said diphenyl compound is administered by intravenous infusion of a solution thereof over a period of time of up to about 90 minutes prior to administration of said chemotherapeutic agents and is maintained during administration of said chemotherapeutic agents.
- 11. The method of claim 10 wherein said diphenyl compound is administered for about 60 minutes prior to administration of said chemotherapeutic agents and is maintained during intravenous infusion of said chemotherapeutic agents.
- 12. The method of claim 11 wherein administration of taxane chemotherapeutic agent, optionally in combination with anthracycline chemotherapeutic agent, is effected during about 20 minutes maintenance of infusion of diphenyl compound, followed by continued infusion of diphenyl compound for the remainder of the administration of the taxane chemotherapeutic agent.
- 13. The method of claim 8 wherein said diphenyl compound is administered in an amount of about 8 to about 240 mg/M² of said patient.
- 14. The method of claim 13 wherein said amount is about 3 to about 10 mg/kg of patient.
- 15. The method of claim 10 wherein said diphenyl compound is administered in an amount of about 3 to about 10 mg/kg of patient.

WO 2004/022163 PCT/CA2003/001335

12

- 16. The method of claim 11 wherein said diphenyl compound is administered in an amount of about 6 mg/kg.
- 17. The method of claim 16 wherein said chemotherapeutic agents are administered in an amount of about 50 to about 60 mg/M² of patient for doxorubicin or epirubicin, about 175 to about 225 mg/M² for Taxol and about 75 to about 100 mg/M² of Taxotere.
- 18. The method of claim 16 wherein said anthracycline chemotherapeutic agent is doxorubicin or epirubicin administered in an amount of 50 mg/M² and said taxane therapeutic agent is Taxol administered in an amount of 175 mg/M² or Taxotere is administered in an amount of 75 mg/M².
- 19. The method of claim 1 wherein the number of cycles of chemotherapy treatment is about 5 to about 10 administered at intervals of about 21 to about 28 days.